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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/774,144
Filing Date: February 06, 2004
Appellant(s): HICKOK ET AL.

Theodore R. Allen
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 30 March 2009 and the supplemental appeal brief filed 29 June 2009 appealing from the Office action mailed 29 July 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

WO 94/17405 (LEAVITT et al.) 04 August 1994.

JOHNSON et al. "Efficacy of 17alpha-hydroxyprogesterone caproate in the prevention of premature labor" The New England Journal of Medicine, vol. 293, no. 14 (02 October 1975), pp. 675-680.

MEIS et al. "17 alpha hydroxyprogesterone caproate prevents recurrent preterm birth" American Journal of Obstetrics and Gynecology, vol. 187 (2002), p. S54.

KEIRSE, M.J.N.C. "Progestogen administration in pregnancy may prevent preterm delivery" British Journal of Obstetrics and Gynaecology, vol. 97 (February 1990), pp. 149-154.

DA FONSECA et al. "Prophylactic administration of progesterone by vaginal suppository to reduce the incidence of spontaneous preterm birth in women at increased risk: a randomized placebo-controlled double-blind study" American Journal of Obstetrics and Gynecology, vol. 188, no. 2 (February 2003), pp. 419-424.

GOLDSTEIN et al. "A meta-analysis of randomized control trials of progestational agents in pregnancy" British Journal of Obstetrics and Gynaecology, vol. 96 (March 1989), pp. 265-274.

YEMINI et al. "Prevention of premature labor by 17alpha-hydroxyprogesterone caproate" American Journal of Obstetrics and Gynecology, vol. 151, no. 5 (March 1, 1985), pp. 574-577.

ANDERSEN et al. "Preterm labor" in Danforth's Obstetrics and Gynecology, 6th Edition (L. McAllister et al., eds.), published 1990 by J.B. Lippincott Company, Philadelphia, pp. 335-351.

WEINER et al. "The therapeutic efficacy and cost-effectiveness of aggressive tocolysis for premature labor associated with premature rupture of the membranes" American Journal of Obstetrics and Gynecology, vol. 159, no. 1 (July 1988), pp. 216-222.

ALLEN et al. "The role of n-3 fatty acids in gestation and parturition" Experimental Biology and Medicine, vil. 226, no. 6 (2001), pp. 498-506.

OLSEN et al. "Randomized controlled trial of effect of fish-oil supplementation on pregnancy duration" The Lancet, vol. 339, no. 8800 (April 25, 1992), pp. 1003-1007.

5,211,952	SPICER et al.	5-1993
5,321,044	PETERS et al.	6-1994

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Under 35 U.S.C. 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 67-76, 79, and 81-94 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope with these claims.

The prior art would suggest that an ability to prolong a pregnancy at risk for preterm delivery is not a property known or common to the generic list (see pages 10-12) of progestational agents disclosed by appellant (see e.g. Goldstein et al. and Keirse in this regard). "[T]here are large differences among the many agents considered to be progestational on the basis of pharmacological tests" (Keirse, page 149), including differences in teratogenic, metabolic, or hemodynamic effects of natural progesterone compared to artificial progestagens (da Fonseca et al., page 419) as well as differences specifically in their ability to reduce the occurrence of preterm birth, prompting Keirse to limit the analysis to a particular agent and reach a different conclusion than in the generic analysis of Goldstein et al. (see e.g. Keirse, page 153, col. 2). Many agents are considered to be progestational on the basis of pharmacological tests, yet the results of the use of progestational agents, such as progesterone-related agents, generally for prolonging a pregnancy at risk for preterm delivery, the only reason for its use in the instant specification (see e.g. pages 1-3 or 6), would seem unknown and unpredictable because only specific agents were tested and suggested to have that ability (see e.g. Goldstein et al. or Keirse or da Fonseca et al. or Meis et al.). The specification merely suggests the use of agents that retain the activity of progesterone to inhibit or delay delivery (see pages 10-12), but provides no guidance for which agents retain such activity. Appellant has provided nothing on the record to predictably link the use of a generic progestational agent, such as those progesterone-related

agents or other agents listed in the specification, as a contraceptive (i.e., **preventing** a pregnancy, as in Spicer et al. (US 5,211,952, cited at specification page 11) or Peters et al. (US 5,321,044, cited in appellant's response filed 18 August 2006)) to its successful use as an agent for **prolonging** a pregnancy at risk for preterm delivery. It is also noted that appellant's specification provides no working examples of pregnancy prolongation other than that demonstrated in the art with progesterone (da Fonseca et al.) or 17α-hydroxyprogesterone (Johnson et al., Yemini et al., Keirse, or Meis et al.) or omega-3 fatty acid supplementation (Allen et al. or Olsen et al.). Random experimentation unguided by appellant to determine progestational agents that do or do not function in the invention suggested by appellant's specification is undue experimentation. Absent further guidance from appellant, and such random unguided undue experimentation, one would not be assured of the ability to practice the invention commensurate in scope with these claims.

Claims 67-94 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regard to these claims, the specification, as originally filed, does not provide support for the patient population as is now claimed. Although the methods can be used with any pregnant patient, appellant teaches monitoring the level of markers particularly in patients with risk factors for preterm delivery, a patient displaying specific symptoms being among those listed risk factors (see e.g. specification pages 18-19). Thus, appellant specifically teaches that

patients with risk factors **should** be tested and that specific symptoms were among these risk factors indicative of testing. Appellant provides no written description that only patients with risk factors not including symptoms should be tested to the exclusion of those with symptoms as is now claimed. Moreover, appellant does not define, and one would not readily know absent further guidance from appellant, what patients are encompassed by the current criteria of "asymptomatic" because only a short inclusive list of possible symptoms is taught. Although one of skill in the art might realize from reading the disclosure that any pregnant patient is useable in the invention, such possibility of use does not provide explicit or implicit indication to one of skill in the art that **only** "asymptomatic" patients were originally contemplated as part of appellant's invention and such possibility of use does not satisfy the written description requirements of 35 U.S.C. § 112, first paragraph. Note that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement.

Appellant was requested to direct the Examiner's attention to specific passages where support for these newly recited limitations can be found in the specification as filed or was required to delete the new matter.

Under 35 U.S.C. 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 67-94 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which appellant regards as the invention.

In claims 67-94, "the" level lacks antecedent basis.

In claim 68, "the" locations lack antecedent basis. In this claim, improper Markush language is used to claim the members of the group. The alternatives "or" or "selected from the group consisting of...and" are acceptable.

In claim 71, "the" start lacks antecedent basis.

In claim 75, "the" onset lacks antecedent basis.

In claim 80, ".alpha." is not clear.

In claim 81, "the" therapeutically effective amount lacks antecedent basis.

In claim 83, it is not clear if "the" sample is the same sample tested in claim 67 or a newly obtained sample.

In claims 85 or 86, "the" locations lack antecedent basis.

In claim 87 and claims dependent thereupon, the interrelationships of the steps are not clear because it is not clear if the contacted sample of step a) is that contacted in step b).

In claim 91 and claims dependent thereupon, it is not clear how detection of a complex with anti-fibronectin antibody specifically detects fetal fibronectin.

In claim 92, the interrelationships of the steps are not clear because it is not clear if the contacted sample of step a) is that contacted in step c).

Under 35 U.S.C. 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned

at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 67-76 and 79-94 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Leavitt et al. (WO 94/17405) in view of any of Johnson et al. (NEJM 293: 675, 1975), Meis et al. (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990), and further in view of Weiner et al. or Andersen et al. for reasons of record repeated below.

The invention as instantly disclosed, with regard to determinations of fetal fibronectin (i.e. a fetal restricted antigen, see instant specification page 2) or total fibronectin as biochemical markers of impending imminent preterm delivery and of insulin-like growth factor binding protein-1 to determine fetal membrane status to aid clinical decisions regarding administration of treatments to prolong pregnancy in pregnant patients at 12 to 37 weeks gestation (see e.g. pages 3-6, 8), is essentially as disclosed and claimed in the reference of Leavitt et al. (except for the instantly disclosed, and no longer claimed, alternative use of estriol determination as a biochemical marker of impending preterm labor). In contrast to the invention as instantly disclosed and claimed, Leavitt et al. does not teach the specific use of progestational agents as the agents to prolong the pregnancy determined to be at risk for preterm delivery in the absence of ruptured membranes.

Any of Johnson et al. (NEJM 293: 675, 1975), Meis et al. (Am. J. Obstet. Gynecol. 187: S54, 2002), or Keirse (Br. J. Obstet. Gynaecol. 97: 149, 1990) teach the efficacy of progesterone treatments in reducing preterm delivery.

Weiner et al. or Andersen et al. teach that treatment with tocolytic agents is not beneficial (Weiner et al.) and not recommended (Andersen et al., page 346; Weiner et al.) in patients with rupture of membranes. Progestational agents are known as among the tocolytic agents that

function to **prevent** or reduce contractions prior to preterm labor (see e.g. Andersen et al. (page 345)).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have tested a pregnant patient determined to have biochemical markers indicative of impending preterm delivery for the status of the fetal membranes and to treat those patients with intact fetal membranes indicated as at risk of having impending delivery with a pregnancy-prolonging agent because of the direct suggestion in Leavitt et al. to do so. One of ordinary skill would have had ample motivation to determine and/or confirm fetal membrane rupture in patients with impending delivery, as determined by any method, because determination of ruptured fetal membranes is of unquestioned importance relating to the health of both the mother and the fetus and for the clinical management of pregnant patients, particularly in those patients at risk for preterm birth wherein a decision regarding the use of tocolytic/pregnancy-prolonging agents must be weighed (Leavitt et al., Weiner et al., or Andersen et al.). One would have been motivated to treat a patient so identified with a known efficacious pregnancy-prolonging agent, such as the progesterones as taught by any of Johnson et al., Meis et al., or Keirse, in view of the direct suggestion to do so in Leavitt et al. and because one would have had an extremely reasonable expectation that a known efficacious pregnancy-prolonging agent would successfully perform its desired function in the method. It would have been obvious to formulate the reagents required to perform the method of Leavitt et al., as modified, into a kit since that is conventional for convenience, reproducibility, and economy.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claims 77 and 78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leavitt et al., in view of any of Johnson et al., Meis et al., or Keirse, and further in view of Weiner et al. or Andersen et al., as applied to claims 67-76 and 79-94 above, and further in view of Allen et al. (Exp. Biol. Med. 226: 498, 2001) or Olsen et al. (Lancet 339: 1003, 1992).

The teachings of Leavitt et al., Johnson et al., Meis et al., Keirse, Weiner et al., and Andersen et al. are as set forth above and differ from the invention as instantly claimed in not teaching omega-3 fatty acids as a pregnancy-prolonging agent.

Either of Allen et al. or Olsen et al. teach the efficacy of omega-3 fatty acid supplementation treatments in reducing preterm delivery.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have supplemented the diet of those patients with intact fetal membranes indicated as at risk of having impending delivery with a pregnancy-prolonging agent because of the direct suggestion in Leavitt et al., as modified, to do so. One would have been motivated to treat a patient so identified with a known efficacious pregnancy-prolonging agent, such as omega-3 fatty acids as taught by either of Allen et al. or Olsen et al., in view of the direct suggestion to do so in Leavitt et al., as modified, and because one would have had an extremely reasonable expectation that a known efficacious pregnancy-prolonging agent would successfully perform its desired function of prolonging pregnancy in the method. It would have been further obvious to have administered a plurality of pregnancy-prolonging agents to the identified patients for the combined benefits of each agent.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

(10) Response to Argument

Under 35 U.S.C. 112, First Paragraph

Appellant's arguments have been fully considered but they are not deemed to be persuasive.

Appellant urges that all of the method steps are described by the specification. This is not in dispute. Appellant's arguments were not found persuasive because the rejection of claims 67-76, 79, and 81-94 under 35 U.S.C. 112, first paragraph, that is Issue 1, is made under the enablement provisions of 35 U.S.C. 112, first paragraph, not under the written description provisions of the statute as argued by appellant. The issue is, as set forth in the rejection, whether one would be assured of the ability to practice the invention commensurate in scope with these claims with the full scope of the listed genus of progestational agents in view of the suggestions in the prior art of the unpredictability that progestational agents other than progesterone or 17α-hydroxyprogesterone or agents other than omega-3 fatty acid supplementation function for prolongation of a pregnancy at risk for preterm delivery. The analysis of Keirse, compared to the analysis of Goldstein et al., suggested to Keirse that the different conclusions reached may have been the result of the heterogeneity of the progestational treatments analyzed by Goldstein et al., that is, too wide a divergence in the structures analyzed by Goldstein et al. led to a conclusion by that reference that the genus did not significantly function in contrast to an analysis performed with a single member of the genus. Moreover,

appellant's list of progestational agents is based upon agents which function for contraception and, as set forth, there is nothing in evidence that any of these agents, other than those specifically taught in the prior art, function as desired in the instant invention for prolongation of pregnancy absent further unpredictable experimentation to determine which of the listed agents function and which do not. Random experimentation with no predictability of success to determine that which is functional is undue experimentation and is not found to provide an enabling disclosure.

Appellant urges that setting forth at least two functional examples in the specification, examples based upon the showings in the prior art, are sufficient to enable the genus. This is not found persuasive for the reasons set forth in the rejection of these claims because the ability of other members of the genus to function is unknown and unpredictable as suggested by the cited prior art. It is noted that claims limited to those agents found functional by the prior art were not rejected under the instant grounds of rejection. However, the unsupported generic claims remain rejected.

With regard to Issue 2, appellant urges that appellant contemplated a lack of symptoms as being a significant problem associated with preterm delivery, that risk factors associated with preterm delivery include risks without symptoms, and that such women without symptoms were contemplated for testing with the method. This is not found persuasive for the reasons of record and as set forth above. Appellant teaches that certain symptoms, among other indicators, indicate a risk of preterm delivery and that those patients with such factors of risk of preterm delivery should be tested with the method. If those patients with risks should be tested, those patients with symptoms should be tested, and the examiner questions where in the specification it

is taught that patients with only one of many listed risk factors which should be tested are now to be singled out for exclusion from testing. The disclosure that a certain entire group of patients should be tested is not found to support the now implied exclusion of a subgroup from the test group. Such is considered new matter unsupported by the disclosure as filed.

Under 35 U.S.C. 112, Second Paragraph

Appellant's arguments have been fully considered but they are not deemed to be persuasive.

Appellant urges that the after final amendment which proposed corrections for many of the issues under 35 U.S.C. 112, second paragraph, was not entered by the examiner. This is true because the amendment also raised new issues, unrelated to the instant issues under 35 U.S.C. 112, second paragraph, which would have required further consideration under both 35 U.S.C. 112, first and second paragraphs, and the amendment was denied entry at least for that reason as noted on the Advisory action mailed 25 November 2008. As the proposed amendments were not entered, the rejections of record stand. Appellant was not denied the opportunity to submit additional amendments to address the outstanding issues under 35 U.S.C. 112, second paragraph, without the raising of new issues before the filing of appellant's brief.

Under 35 U.S.C. 103

Appellant's arguments have been fully considered but they are not deemed to be persuasive.

Appellant urges that the disclosure in the reference of Leavitt et al., or in any of the secondary references, does not support the limitation of obtaining a sample from a subject who is asymptomatic as is now claimed. This is not found persuasive for the reasons of record because the disclosure to which appellant points as supporting this limitation, the paragraph bridging pages 18-19 of the specification, is taken essentially verbatim from the disclosure of Leavitt et al. at page 6 of the document and therefore the reference is found to support testing the exact same patient populations with or without the exact same risk factors for preterm delivery. If, as asserted by appellant, the passage supports the testing of patients having risk factors other than symptoms, i.e. asymptomatic patients, in the instant specification the essentially same disclosure in the reference supports the identical patient population. It is also noted that the reference of Leavitt et al. teaches the performance of the method in "a pregnant patient" (see e.g. page 4) and that this would necessarily include both symptomatic and asymptomatic patients. As set forth in the rejection of record, the disclosure of the testing portion of the method is essentially as taught in the reference of Leavitt et al.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/JAMES L GRUN/

Examiner, Art Unit 1641

Conferees:

/Mark L. Shibuya/

Supervisory Patent Examiner, Art Unit 1641

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Supervisory Patent Examiner, Art Unit 1649